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Correlation between *Prevotella intermedia* and intraoral metal alloys

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Objective: We investigated the potential association between intraoral metal alloys and the presence of *Prevotella intermedia* in patients with rheumatoid arthritis (RA). **Methods:** A case-control study was conducted using bacteriological tests. The RA group included 80 patients, of whom 40 tested positive for *Prevotella intermedia* and 40 tested negative. The control group consisted of 81 subjects without RA, with 39 testing positive for *Prevotella intermedia* and 42 testing negative. **Results:** Univariate analysis identified the presence of intraoral metal alloys (lingual fixed retainers or metal-ceramic crowns), male sex, and gingival inflammation as significant predictors of *Prevotella intermedia* presence ($P < 0.05$). In multivariate analysis, intraoral metal alloys demonstrated the strongest association, with an odds ratio = 4.21 ($P < 0.001$). However, no significant difference in *Prevotella intermedia* positivity was observed between the RA and control groups. **Conclusions:** These findings suggest that intraoral metal alloys are associated with an increased prevalence of *Prevotella intermedia* in subgingival pockets among adults, independent of RA status.

Key words: Oral dysbiosis, *Prevotella intermedia*, Intraoral metal alloys, Rheumatoid arthritis

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INTRODUCTION

The oral microbiota plays a significant role in maintaining oral health. Over time, under specific conditions, oral dysbiosis can occur, leading to various oral pathologies such as dental caries, periodontitis, and periimplantitis.^{1,2} Additionally, changes in host factors and immune responses may alter the virulence of oral pathogens, reshaping the oral microenvironment.^{1,3} For example, a research has demonstrated that certain ceramic surfaces used in dental treatments may promote the growth of *Prevotella intermedia*, a known periodontal pathogen.⁴

This is particularly relevant due to its implications for both oral and systemic health. A clinical study has suggested a possible link between the pathogenicity of certain oral bacteria and rheumatoid arthritis (RA), a systemic autoimmune disease characterized by immune system dysfunction.⁵ Both conditions share common risk factors: oral bacteria may contribute to RA pathogenesis, while RA may increase susceptibility to periodontitis.⁶

The colonization of dental materials composed of metal alloys by oral bacteria is influenced by the physical properties of the metal, such as surface roughness. The composition of these materials, including elements such as fluoride, organic matrices, and various metal ions, can either inhibit or enhance biofilm formation.^{7,8} Consequently, long-term use of intraoral metal-containing appliances, such as orthodontic devices, may influence microbial composition in the oral cavity. Mulimani and Popowics⁹ concluded that persistent environmental exposure to orthodontic appliances can modify oral bacterial composition, potentially leading to pathogenicity and the development of oral diseases such as dental caries, enamel demineralization, and periodontitis. In this context, Eliades et al.¹⁰ reported that stainless-steel brackets exhibit a higher plaque-retaining capacity, which may contribute to biofilm accumulation. Recent research has focused on improving the biocompatibility and surface characteristics of orthodontic materials to optimize oral biofilm management.¹¹

We hypothesized that the presence of metal-based crowns from prosthetic appliances or fixed orthodontic retainers could alter the subgingival microbiome, thereby promoting the growth of *Prevotella intermedia*. Our aim was to determine whether these factors serve as predictors of *Prevotella intermedia* colonization, which is associated with periodontitis, and to assess whether RA influences this process.

MATERIALS AND METHODS

We recruited 80 patients diagnosed with RA from a bacteriological sample of 200 patients with RA treated at the Rheumatology Service of the University Hospital of

Santiago de Compostela. Ethical approval was obtained from the Institutional Committee of Clinical Research of Galicia, Spain (Ethics Approval Number 2020/137) before the initiation of this study to ensure adherence to the principles outlined in the Declaration of Helsinki and Tokyo for human research. The study protocol fully complied with these ethical guidelines. Additionally, all participants provided written informed consent for the use of their data in this study. The inclusion criteria for this study were adult patients (> 18 years old) of either sex, diagnosed with RA according to the ACR/EULAR 2010 criteria, and having at least 10 dental pieces.

The study group (n = 80) was divided into two subgroups based on the presence of *Prevotella intermedia*: 40 patients tested positive, while 40 tested negative. The prevalence of *Prevotella intermedia* was statistically analyzed in comparison with various clinical and demographic variables in a healthy control group (n = 81) without RA. Of whom, 42 tested positive for *Prevotella intermedia*, and 39 tested negative.

The following variables were evaluated in this study: sociodemographic characteristics (age, sex), smoking habits, comorbidities (with a primary focus on the presence of metal-alloy dental materials within the oral cavity), and detection of autoantibodies (anti-cyclic citrullinated peptides, rheumatoid factor) in patients with RA (see Supporting Information). Periodontal parameters were also recorded, including periodontal pocket depth (PD) measured in millimeters and bleeding on probing (yes/no). Periodontal probing was performed using a periodontal probe (Williams probe, Chicago, IL, USA) to measure the periodontal PD at designated sites. Measurements were taken at specific points of interest, including dental pieces with prosthetic restorations and those adjacent to the retention wires. Periodontal PD was categorized into three stages: PD ≤ 3 mm (Grade 0), 3 mm < PD < 6 mm (Grade 1), and PD ≥ 6 mm (Grade 2) (see Supplementary Material for this and other details about patients and controls).

To identify subgingival bacteria composition, a molecular analysis was conducted using polymerase chain reaction. Five periodontal pathogens in the gingival pocket were identified and quantified (*Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythea*, *Treponema denticola*, and *Prevotella intermedia*).

RESULTS

No significant difference in *Prevotella intermedia* positivity was observed between healthy individuals and those with RA.

The association between *Prevotella intermedia* and comorbidities was assessed using logistic regression,

with results expressed as odds ratios (ORs) and 95% confidence intervals (CIs). All statistical analyses were conducted using Stata 17.0 (Stata Corporation, College Station, TX, USA).

Univariate analysis identified the presence of external dental materials, male sex, and periodontal pocket (measured in PD) as significant predictors of *Prevotella intermedia* positivity. Multivariate analysis further confirmed these associations, with dental materials showing the strongest correlation. In patients with RA, the presence of dental material was associated with an OR of 4.05 ($P < 0.001$), while in the control group, the OR was 4.21 (Tables 1 and 2).

The effect of age on *Prevotella intermedia* positivity was examined using multivariate analysis; however, the association was not statistically significant ($P = 0.317$). The OR for age was 1.00 (95% CI: 0.99–1.02, $P = 0.317$), indicating no meaningful relationship between age and *Prevotella intermedia* prevalence in this sample.

Although analyzing bacterial co-occurrence patterns could provide further insights, the scope of this study did not allow for such an extensive investigation. Therefore, we simply presented observations in this section based on the available data. The presence of *Porphy-*

romonas gingivalis was significantly higher in subjects who tested positive for *Prevotella intermedia* (Table 3) compared to those in whom *Prevotella intermedia* was absent from the periodontal pocket. At this point, it is important to highlight the findings of Kamaguchi et al.,¹² who investigated the hierarchical interactions among oral bacteria. Their study demonstrated that *Porphyromonas gingivalis* cells can co-aggregate with *Prevotella intermedia*, which acts as an early colonizer. This co-aggregation occurs not only in infected gingival crevices but also in the normal gingival crevices.¹²

DISCUSSION

This study highlights the impact of external factors, specifically metal-based alloys from dental treatments, on subgingival microbial colonization. Several studies have explored this relationship. Rademacher et al.¹³ reported that surface structure modifications, increased roughness, enhanced bacterial retention, galvanic corrosion, and metal leakage from diverse dental materials can influence microbial composition. Similarly, Alarcón-Sánchez et al.¹⁴ reviewed the effects of dental prosthetic materials on periodontal tissues, concluding that metal-ceramic prostheses contribute to a more dysbiotic biofilm with an increased prevalence of periodontopathogenic bacteria. Guo et al.¹⁵ further emphasized the need to consider the effect of dental prosthetic materials on the oral microbiome, highlighting the potential for oral bacteria to induce biological corrosion on these materials, particularly when they remain in the mouth for a prolonged period. Notably, dental materials containing metal components can remain in the oral cavity for several years,¹⁶ as is the case with implants, crowns, or fixed orthodontics retainers.

In alignment with these studies, we identified a statistically significant association (OR = 4.21, $P < 0.001$) between metal-containing oral environments and *Prevotella intermedia* presence. Orthodontic appliances have also

Table 1. Multivariate analysis for predicting the presence of *Prevotella intermedia* in patients with rheumatoid arthritis based on variables, including the presence of metal alloys in the mouth, male sex, and periodontal pocket depth

Study group (<i>Prevotella intermedia</i>)	OR	CI 95%	P value
Metal	4.05	2.05–8.01	< 0.001
Sex	0.50	0.25–0.99	0.048
Pocket (mm)	1.80	1.11–2.90	0.016

Results are presented as odds ratio (OR), 95% confidence intervals (CIs), and P value.

Table 2. Multivariate analysis of the control group for predicting the presence of *Prevotella intermedia* based on variables, including the presence of metal alloys in the mouth, male sex, and periodontal pocket depth

Control group (<i>Prevotella intermedia</i>)	OR	CI 95%	P value
Metal	4.21	2.07–8.57	< 0.001
Sex	0.43	0.20–0.92	0.030
Pocket (mm)	1.77	1.05–2.97	0.031

Results are presented as odds ratio (OR), 95% confidence intervals (CIs), and P value.

Table 3. Number of patients and controls with or without combination of *Porphyromonas gingivalis* and *Prevotella intermedia*

	Rheumatoid arthritis	Control
<i>Porphyromonas gingivalis</i> + & <i>Prevotella intermedia</i> -*	7	7
<i>Porphyromonas gingivalis</i> + & <i>Prevotella intermedia</i> +†	22	21

*Number of patients and controls positive for *Porphyromonas gingivalis* and negative for *Prevotella intermedia*.

†Number of patients and controls positive for *Porphyromonas gingivalis* and positive for *Prevotella intermedia*.

been shown to alter oral microbiota composition.^{17,18} Al-Ali and Al Groosh¹⁹ concluded that fixed retainers and other orthodontic appliances may increase the colonization of cariogenic and periodontal pathogens, potentially compromising oral health. Our findings align with these studies, as we demonstrated that the presence of metals (e.g., in the lower fixed retainers) is associated with an increased prevalence of *Prevotella intermedia*.

A limitation of our study is that we did not analyze the variables independently or assess the specific composition of the metal structures used. Instead, we collected samples from oral areas containing metal alloys and evaluated whether their presence was associated with an increased total abundance of *Prevotella intermedia*. To account for potential confounders, we performed multivariate logistic regression modeling, adjusting for factors such as age and sex. After adjustment, metal presence remained significantly associated with *Prevotella intermedia* (OR = 4.05, $P = 0.001$ in patients with RA, and OR = 4.21 in the control group). We found that the oral presence of *Prevotella intermedia* was the same in patients with and without RA. However, whether the presence of metals in the mouths of patients with RA, identified as a potential dysbiosis-inducing factor in this study, could contribute to the progression or severity of RA over time remains unknown.

Univariate analysis identified male sex as a predictor of *Prevotella intermedia* positivity (OR = 0.50, $P = 0.048$ in patients with RA; OR = 0.43, $P = 0.033$ in the control group). Consistent with this, Zhao et al.²⁰ reported that sex influences subgingival bacterial composition in adult patients (aged 50–68 years) with early-stage periodontitis. Additionally, univariate analysis revealed an association between *Prevotella intermedia* presence and periodontal pockets ≥ 6 mm in depth.

A diverse microbiome is generally considered a marker of oral health; however, microbial composition changes with age, leading to reduced diversity and an increased prevalence of pathogenic bacteria.²¹ In this study, no significant correlation was observed between age and the presence of *Prevotella intermedia* in the gingival pocket.

CONCLUSIONS

The presence of metal alloys in the oral environment was significantly associated with an increased prevalence of *Prevotella intermedia* in the subgingival pocket of adult patients, regardless of RA status. These findings highlight the importance of considering biocompatibility and biofilm formation potential when selecting dental materials. Assessing bacterial activity in the oral cavity is clinically relevant, as all dental materials are continuously exposed to a complex microbial environment.

AUTHOR CONTRIBUTIONS

Conceptualization: MFO, AMV, JM. Data curation: MFO, RDS, EPP. Formal analysis: RDS. Investigation: MFO, JM. Methodology: MFO, RDS, EPP. Project administration: JM. Supervision: AMV, JM. Validation: AMV, JM. Writing—original draft: MFO, JM. Writing—review & editing: RDS, EPP, AMV.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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None to declare.

SUPPLEMENTARY MATERIAL

Supplementary data is available at <https://doi.org/10.4041/kjod25.015>

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